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15/54, C12Q 1/48, G01N 33/50, 33/53, A61K 39/00, 38/00

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60/406,936 30 August 2002 (30.08.2002) US

(71) Applicant (for all designated States except US): **BAYER AKTIENGESELLSCHAFT** [DE/DE]; 51368 Leverkusen (DE).

(72) Inventor; and

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(74) Common Representative: **BAYER AKTIENGESELLSCHAFT**; 51368 Leverkusen (DE).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

**Published:**

- without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **REGULATION OF HUMAN BMP-2 INDUCIBLE KINASE**

(57) Abstract: Reagents that regulate human BMP-2 inducible kinase and reagents which bind to human BMP-2 inducible kinase gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, cancer, diabetes, CNS disorders, COPD, gastrointestinal disorders, and cardiovascular disorders.

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(75) Inventor/Applicant (for US only): **LIU, Jiling-Ren** [CN/US]; 10 Winslow Road, Belmont Road, MA 02478 (US).

(74) Common Representative: **BAYER HEALTHCARE AG**; Law and Patents, Patents and Licensing, 51368 Leverkusen (DE).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **FURTHER BMP-2 INDUCIBLE KINASES AND THE USES THEREOF**

(57) Abstract: Reagents that regulate human BMP-2 inducible kinase and reagents which bind to human BMP-2 inducible kinase gene products may play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, cancer, diabetes, CNS disorders, COPD, gastrointestinal disorders, and cardiovascular disorders.

WO 2003/080825 A3

# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/EP 02902

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N9/12 C12N15/54 C12Q1/48 G01N33/50 G01N33/53  
A61K39/00 A61K38/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q G01N A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, EPO-Internal, EMBL, BIOSIS, WPI Data, PAJ, CHEM ABS Data, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 00 21976 A (GEN HOSPITAL CORP) 20 April 2000 (2000-04-20) abstract SEQ ID NO.: 2 page 4, line 21 - line 27 page 18, line 24, FF. page 23, line 13, FF. page 33; claims 3-22</p> <p style="text-align: center;">-/--</p>	1-17

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

17 September 2003

Date of mailing of the international search report

2. 12. 03

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Publication No.

PCT/EP 00/02902

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>KEARNS A E ET AL: "Cloning and characterization of a novel protein kinase that impairs osteoblast differentiation in vitro."  THE JOURNAL OF BIOLOGICAL CHEMISTRY.  UNITED STATES 9 NOV 2001,  vol. 276, no. 45,  9 November 2001 (2001-11-09), pages  42213-42218, XP002250920  ISSN: 0021-9258  abstract  page 42215; figure 2  Introduction  page 42213 -page 42214  Discussion  page 42217 -page 42218</p>	1-17
X	<p>WO 01 77150 A (MERCK PATENT GMBH ;GUESSOW  DETLEF (DE); SCHARM BURKHARD (DE))  18 October 2001 (2001-10-18)  SEQ ID NOs: 3 and 4  abstract</p>	1-17
X	<p>WO 01 53312 A (CHEN RUI HONG ;GOODRICH  RYLE (US); HYSEQ INC (US); WANG DUNRUI  (US) 26 July 2001 (2001-07-26)  SEQ ID NO.: 2577</p>	1-17
X	<p>WO 01 38503 A (PLOWMAN GREGORY D ;CLARY  DOUGLAS (US); SUGEN INC (US); WHYTE DAVID)  31 May 2001 (2001-05-31)  Protein SGK419 ID#AA92</p>	1-17
X,P	<p>WO 02 083709 A (TANG Y TOM;INCYTE GENOMICS  INC ; RECIPON SHIRLEY A (US); BURRILL J)  24 October 2002 (2002-10-24)  abstract  page 102; table 2  SEQ ID NOS: 1 AND 16</p>	1-17
X,P	<p>DATABASE EMBL 'Online!  EBI; 24 September 2002 (2002-09-24)  STRAUSBERG: "Homo sapiens, Similar to  BMP-2 inducible kinase"  retrieved from EMBL  Database accession no. BC036021  XP002250921  the whole document</p>	1-17

# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/EP 03/02902

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☒ Claims Nos.: 8,9,13-17(partly)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-17 (partly)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 8,9,13-17(partly)

Present claims 8,9,13-17 relate to a compound/method defined by reference to a desirable characteristic or property, namely to reagent which specifically interacts with polypeptide or polynucleotide of BMP-2 inducible kinase or modulate the activity thereof

The claims cover all methods/componds/uses having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds/methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound/method/uses by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds which are specific antibodies and anti-sense poly-/oligo-nucleoties.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

## 1. Claims: 1-17(partly)

An isolated polynucleotide being selected from the group consisting of: a polynucleotide encoding BMP-2 inducible kinase polypeptide comprising an amino acid sequence selected from the group consisting of:

- a)
  - i. amino acid sequences which are at least 72% identical to the amino acid sequence shown in SEQ ID NO.: 2 and
  - ii. the amino acid sequence shown in SEQ ID NO.: 2
- b)  
a polynucleotide comprising the sequence of SEQ ID NOs: 1 or 3
- c)  
a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in a) and b), and which encodes said amino acid sequences;
- d)  
a polynucleotide the sequence of which deviates from from the polynucleotide sequence specified above due to the degeneration of the genetic code and which encodes said amino acid sequence;
- e)  
a polynucleotide which represents a fragment, derivative or allelic variation of the polynucleotide specified above and which encodes said amino acid sequence.

The subject matter of dependent claims 2-17 in relation of the isolated polynucleotide as above.

## 2. Claims: 1-17(partly)

An isolated polynucleotide being selected from the group consisting of: a polynucleotide encoding BMP-2 inducible kinase polypeptide comprising an amino acid sequence selected from the group consisting of:

- a)
  - i. amino acid sequences which are at least 72% identical to the amino acid sequence shown in SEQ ID NO.: 4 and
  - ii. the amino acid sequence shown in SEQ ID NO.: 4
- b)  
a polynucleotide which hybridises under stringent conditions

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

to a polynucleotide specified in a), and which encodes said amino acid sequences;

c)

a polynucleotide the sequence of which deviates from from the polynucleotide sequence specified above due to the degeneration of the genetic code and which encodes said amino acid sequence;

d)

a polynucleotide which represents a fragment, derivative or allelic variation of the polynucleotide specified above and which encodes said amino acid sequence.

The subject matter of dependent claims 2-17 in relation to the isolated polynucleotide as above.



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02902

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0021976	A	20-04-2000	AU 6519299 A CA 2345885 A1 EP 1121374 A1 JP 2002527053 T WO 0021976 A1	01-05-2000 20-04-2000 08-08-2001 27-08-2002 20-04-2000
WO 0177150	A	18-10-2001	CA 2405730 A1 WO 0177150 A2 EP 1272641 A2 JP 2003530122 T	18-10-2001 18-10-2001 08-01-2003 14-10-2003
WO 0153312	A	26-07-2001	US 6569662 B1 AU 2292401 A AU 2591801 A AU 2593601 A AU 2595501 A AU 2596501 A AU 2598301 A AU 2728401 A AU 2734401 A AU 2734801 A AU 2738501 A AU 3265701 A CA 2395443 A1 CA 2395731 A1 CA 2395736 A1 CA 2395749 A1 CA 2395763 A1 CA 2395770 A1 CA 2402563 A1 EP 1242596 A1 EP 1240178 A2 EP 1242580 A1 EP 1242443 A1 EP 1250346 A2 EP 1254256 A2 EP 1248848 A1 WO 0153312 A1 WO 0153453 A2 WO 0153326 A1 WO 0153454 A2 WO 0153455 A2 WO 0153456 A2 WO 0153466 A1 WO 0152616 A2 WO 0153500 A1 WO 0153515 A1 WO 0153485 A1 US 2003104529 A1 US 2003211987 A1 US 6586390 B1 US 6465620 B1 US 2002146692 A1 AU 5362001 A CA 2406039 A1 EP 1276754 A2 WO 0179446 A2 US 2002197679 A1	27-05-2003 31-07-2001 31-07-2001 31-07-2001 31-07-2001 31-07-2001 31-07-2001 31-07-2001 31-07-2001 31-07-2001 31-07-2001 31-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 25-09-2002 18-09-2002 25-09-2002 25-09-2002 23-10-2002 06-11-2002 16-10-2002 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 26-07-2001 05-06-2003 13-11-2003 01-07-2003 15-10-2002 10-10-2002 30-10-2001 25-10-2001 22-01-2003 25-10-2001 26-12-2002

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Information on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0153312	A		US 2002142953 A1	03-10-2002
WO 0138503	A	31-05-2001	AU 1926001 A	04-06-2001
			CA 2394803 A1	31-05-2001
			EP 1240194 A2	18-09-2002
			JP 2003514583 T	22-04-2003
			WO 0138503 A2	31-05-2001
WO 02083709	A	24-10-2002	WO 02083709 A2	24-10-2002

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